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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,658	04/19/2001	Allan Bradley	11635-004001/ OTA 00-51	9914

7590 02/02/2005

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 02/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/839,658	BRADLEY ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2005 and 06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,17,67 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,17,67 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/7/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to an amendment filed August 30, 2004 and December 6, 2004. Claims 1-14, 17, 67 and 68 were previously pending. Applicants amended claims 1 and 17. Claims 1-14, 17, 67 and 68 are pending and will be examined.

2. Applicants' amendments overcame the following rejections: rejection of claim 17 under 35 U.S.C. 112, second paragraph; rejection of claims 1-8, 12, 13, 17, 67 and 68 under 35 U.S.C. 103(a) over Cronin et al., Salinas-Todo et al., in view of Dorin et al. and Zielenski et al.; rejection of claim 9 under 35 U.S.C. 103(a) over Cronin et al., Salinas-Todo et al., in view of Dorin et al. and Zielenski et al., further in view of Waggoner et al.; rejection of claim 10 under 35 U.S.C. 103(a) over Cronin et al., Salinas-Todo et al., in view of Dorin et al. and Zielenski et al., further in view of Anderson; rejection of claim 11 under 35 U.S.C. 103(a) over Cronin et al., Salinas-Todo et al., in view of Dorin et al. and Zielenski et al., further in view of Ordahl et al. and Anderson.

3. Applicants' amendements necessitated new grounds of rejection presented in this office action. Applicants' arguments are moot in view of new grounds for rejection.

Claim Interpretation

4. With respect to the term "stringent hybridization conditions", Applicants provided the following description (page 13, lines 14-19 and 29-31; page 14, line 1):

> "...The term "stringent conditions" refers to conditions under which a probe will hybridize preferentially to its target subsequence, and to a lesser extent to, or not at all to, other sequences. A "stringent hybridization" and "stringent hybridization wash conditions" in the context of nucleic acid hybridization (e.g., as in array, Southern or Northern hybridizations) are sequence dependent, and are different under different environmental parameters." And

"...However, the selection of a hybridization format is not critical, as is known in the art, it is the stringency of the wash conditions that set forth the conditions which determine whether a nucleic acid is within the scope of the invention."

Therefore, depending on the length of the nucleic acids participating in the hybridization reaction, different conditions will be considered as being "stringent".

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-6, 17, 67 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al. (US 2002/0132246 A1) and McGill et al. (US 5,658,730 A).

Regarding claim 1, Kallioniemi et al. teach detection gene copy number amplifications or deletions by hybridization of target nucleic acids to an array of plurality of immobilized probes by the method comprising:

(a) providing the plurality of nucleic acid probes comprising a plurality of immobilized nucleic acid segments in an array with each probe at a known location, wherein each probe is a member of a genomic library cloned in a vector, and each probe is the vector having a cloned nucleic acid insert greater than about 50 kilobases, wherein the plurality of probes represents all of the chromosome or a genome (Kallioniemi et al. teach CGH (comparative genomic hybridization) arrays (page 2, [0013], [0022]), and DNA arrays in which large-insert genomic clones such as P1, BAC or PAC clones are attached to solid support (page 3, 4 [0053]). Kallioniemi et al. teach an array of clones representing all of the human genome (page 14, [0152], [0153]). Kallioniemi et al.

teach an array of P1, BAC or PAC clones each of which has an insert of 80 to 150 kilobases (page 15, [0156]). Kallioniemi et al. teach an array of clones at known locations (Fig. 14).);

(b) contacting the immobilized probes with a sample of target nucleic acid comprising fragments of genomic nucleic acid labeled with a detectable moiety, wherein each labeled fragment consists of a length smaller than about 200 bases, and the contacting is under conditions allowing hybridization of the target nucleic acid to the probe nucleic acid (Kallioniemi et al. teach contacting genomic DNA target labeled with a fluorescent dye (= detectable moiety) to a CGH array (page 14, [0152]). The target DNA is contacted with the immobilized probes under conditions which permitted hybridization of the target to the probes (page 2, [0016]).); and

(c) observing an amount and location of labeled genomic nucleic acid hybridized to each immobilized probe, to detect regions of amplification or deletion in the sample, wherein positional information of clones on the arrays and chromosomes is correlated, thereby generating a molecular profile of the chromosome or genome of the sample genomic nucleic acid (Kallioniemi et al. teach observation of hybridization events using a CCD camera and detection gene amplifications or deletions on chromosomes (page 2, [0013], [0016]; page 15 [0157], [0160]).).

Regarding claims 12 and 13, Kallioniemi et al. teach hybridization conditions of 42° C and wash of 55° C (page 8, 9, [0100], therefore, according to Applicants' description, they teach stringent hybridization conditions and temperature about 60° C.

Regarding claim 14, Kallioniemi et al. teach target nucleic acid consisting of human DNA (page 14, [0152]).

Regarding claim 17, Kallioniemi et al. teach human genome (page 14, [0153]).

Regarding claims 67 and 68, Kallioniemi et al. teach the sample nucleic acid being total human DNA, therefore anticipating the limitations of a sample comprising at least one chromosome and a sample comprising a complete genome.

B) Kallioniemi et al. do not teach DNA fragments with length of less than about 200 bp to less than about 30 bp.

C) Regarding claims 1-6, McGill et al. teach detection of chromosome 8 amplification using probes derived from the chromosome (col. 3, lines 56-67; col. 4, lines 16). The probe lengths were 10-500 bp (col. 5, lines 35-45 and 52-55), with the optimal probe sequence being about 20 bases (col. 6, lines 1-10).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used short probes of McGill et al. in the hybridization method of Kallioniemi et al. The motivation to do so, provided by McGill et al., would have been that probes with about 20 bases allows formation of duplexes which are stable and selective (col. 6, lines 1-3).

7. Claims 7, 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al. (US 2002/0132246 A1) and McGill et al. (US 5,658,730 A), as applied to claim 1 above, and further in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991; cited in the previous office action).

A) Regarding claim 7, Kallioniemi et al. teach generation of nucleic acids by polymerase chain reaction, nick translation or random priming (page 10, [0114]-[0116].

Regarding claim 8, Kallioniemi et al. teach labeling of nucleic acid fragments by nick translation or random priming (page 10, [0116]).

B) Neither Kallioniemi et al. nor McGill et al. teach fractionation of DNA by DNAse digestion.

C) Anderson teaches fragmentation of genomic DNA to sizes below 200 base pairs by digestion with 2.2 ng or more of DNAse I (Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used DNAse I digestion of Anderson to fragment genomic target DNA in the method of Kallioniemi et al. and McGill et al. The motivation to do so, provided by Anderson, would have been that DNAse I digestion was sequence-independent and the sizes distribution obtained could be regulated by regulating the amount of DNAse I in the reaction (page 3019, first two paragraphs).

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al. (US 2002/0132246 A1) and McGill et al. (US 5,658,730 A), in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1991; cited in the previous office action), as applied to claim 8 above, and further in view of Waggoner et al. (U. S. Patent No. 5,268,486; cited in the previous office action).

A) Claim 9 is drawn to the label comprising Cy3 or Cy5.

B) Kallioniemi et al. and McGill et al. teach fluorescent labels, but do not teach Cy3 or Cy5.

C) Waggoner et al. teach luminescent cyanine dyes, including Cy3 and Cy 5 (col. 19, formula at the bottom; claim 8; Cy3 has m=1, Cy5 has m=2). The dyes are be used to label nucleic acids (col. 2, lines 58-61; col. 4, lines 29-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the cyanine dyes of Waggoner et al. in the method of Kallioniemi et al. and McGill et al. The motivation to do so, provided by Waggoner et al., would have been that cyanine dyes were used for detecting mixtures of components because they had a wide range of excitation and emission wavelengths (col. 4, lines 36-49).

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi et al. (US 2002/0132246 A1) and McGill et al. (US 5,658,730 A), as applied to claim 1 above, and further in view of Ordahl et al. (Nucl. Acids Res., vol. 3, pp. 2985-2999, 1976; cited in the previous office action) and Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1981; cited in the previous office action).

A) Claim 11 is drawn to fragmentation of genomic DNA to sizes smaller than 200 bases by applying shear forces to fragment genomic DNA followed DNAse digestion.

B) Neither Kallioniemi et al. nor McGill et al. teach fragmentation of genomic DNA to sizes smaller than 200 bases by applying shear forces to fragment genomic DNA followed DNAse digestion.

C) Ordahl et al. teach fragmentation of genomic DNA in preparation for DNA hybridization experiments. Ordahl et al. teach that it is advantageous to use DNA fragments of less than 500 bp in hybridization experiments (page 2985, first paragraph). Ordahl et al. teach that DNA fragmented in French press had an average size of 230 base pairs (Abstract; page 2986; Fig. 4). Ordahl et al. do not teach DNAse I fragmentation after shearing.

D) Anderson teaches fragmentation of genomic DNA to sizes below 200 base pairs by digestion with 2.2 ng or more of DNAse I (Figure 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used shearing of Ordahl et al. and DNAse I digestion of Anderson to fragment genomic target DNA in the method of Kallioniemi et al. and McGill et al. The motivation to do so, provided by Ordahl et al. and Anderson, would have been that it was advantageous to use short DNA fragments in hybridization (Ordahl, p. 2885, first paragraph) and that DNAse I digestion was

sequence-independent and the sizes distribution obtained could be regulated by regulating the amount of DNAse I in the reaction (Anderson, page 3019, first two paragraphs).

10. No claims are allowed.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
January 27, 2005

JEFFREY FREDMAN
PRIMARY EXAMINER
1/28/05